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GAP JUNCTIONS MEDIATE AGONIST-INDUCED OSCILLATORY CONTRACTIONS IN VASCULAR SMOOTH MUSCLE

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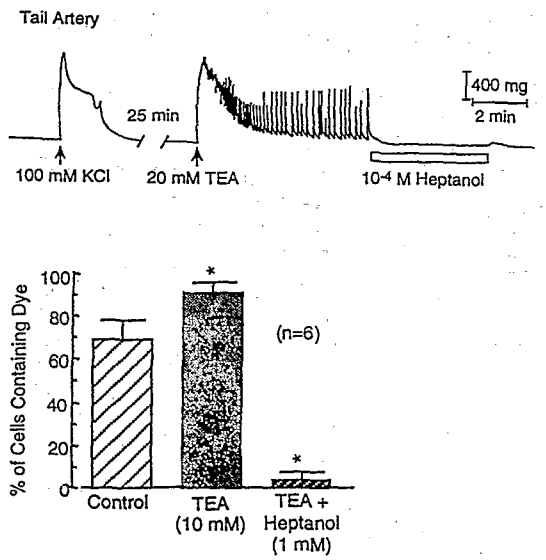
Uterine oscillatory contractions are perpetuated by gap junction complex formation [1]. We tested the hypothesis that agonist-induced oscillations in arteries [2,3] are also mediated by gap junctions. Helical strips of rat mesenteric and tail arteries were mounted in chambers for isometric force measurements. Tetraethylammonium (TEA; 1-30 mM) induced oscillatory contractions that were not endothelium-dependent. Oscillations were blocked by heptanol, a gap junction inhibitor (upper panel). Furthermore, in cultured mesenteric arterial cells, TEA increased Lucifer yellow dye transfer between neighbouring cells, a measure of junctional communication. Heptanol blocked dye transfer (lower panel). These data support a role for gap junction activity in vascular smooth muscle contraction.



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THE CONTRACTILE MECHANISMS OF SODIUM METAVANADATE IN ISOLATED RAT AORTA

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Vanadate and vanadate-containing compounds play important roles in modulating various cellular functions. Structurally similar to phosphate, vanadate has dramatic effects on the activity of many enzymes, either being an inhibitor or a stimulator [1]. Vanadate has been reported to induce contraction of guinea pig aorta, rabbit colon, rat aorta, and canine saphenous vein [2,3]. However, the contractile mechanism of vanadate in smooth muscles has not been well understood. Therefore, in the present study, the mechanism of contractile effect of vanadate was investigated in rat aorta. Sodium metavandate ($NaVO_3$) (10^{-5} M - 3 x 10^{-3} M) induced contractile responses in a concentration-dependent manner. Removal of endothelium did not affect the response to $NaVO_3$. $NaVO_3$ was the most potent agent to cause contraction as compared to vanadyl sulphate (10^{-5} M - 3 x 10^{-3} M) and vanadium trichloride (10^{-5} M - 3 x 10^{-3} M). The response to $NaVO_3$ was inhibited by nifedipine (10^{-6} M), 2-nitro-4-carboxyphenyl-N, N-diphenylcarbamate (NCDC;3 x 10^{-5} M), a phospholipase C inhibitor, and H-7 (10^{-5} M), a protein kinase C inhibitor. The response to $NaVO_3$ was not inhibited by ouabain (10^{-3} M), prazosin (10^{-6} M), an α_1-adrenoceptor inhibitor, methysergide (10^{-6} M), a serotonin receptor inhibitor, tripelennamine (10^{-6} M), a histamine receptor inhibitor, glyburide (10^{-6} M), a K_{ATP} channel blocker, apamin (10^{-6} M), a K_{Ca} channel blocker or Mg^{2+}-removal. In addition, the response to $NaVO_3$ was inhibited by indomethacin (10^{-5} M), a cyclooxygenase inhibitor, and AA861 (10^{-5} M), a 5-lipoxygenase inhibitor. The response to arachidonic acid (10^{-6} M - 3 x 10^{-4} M) was also inhibited by indomethacin (10^{-5} M), AA861 (10^{-5} M), nifedipine (10^{-6} M) and NCDC (3 x 10^{-5} M), but not by H-7 (10^{-5} M). Further, in the presence of indomethacin (10^{-5} M) and AA861 (10^{-5} M), H-7 (10^{-5} M) still inhibited the residual response to $NaVO_3$. In rat aorta, $NaVO_3$ increased the levels of inositol monophosphate (IP) by about 20 time the basal level (control: 147.4± 19.96 cpm/mg wet tissue) and prostaglandin $F_{2\alpha}$ by about 2 times the basal level (control: 88.8±13.6 pg/mg wet tissue). Indomethacin (10^{-5} M), AA861 (10^{-5} M) and NCDC (3 x 10^{-5} M) inhibited the IP increase. Indomethacin (10^{-5} M), but not AA861 (10^{-5} M), also inhibited the $PGF_{2\alpha}$ increase. These results suggest that the response to $NaVO_3$ is due to increased phosphoinositide metabolism and partly to subsequent increase in the metabolism of arachidonic acid.

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